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Cerebellar Pleomorphic Xanthoastrocytoma
- A Case Report -

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Cerebellar pleomorphic xanthoastrocytoma (PXA) is a rare tumor. The most common manifestation of PXA is a seizure, as opposed to the headache and dizziness that were present in our reported case; these atypical symptoms were related to the development of tumor in cerebellum. We describe here a case of PXA in the cerebellum of a 49-year-old female and we discuss the radiological, histological and immunohistochemical findings of PXA that occurred in the cerebellum.

Key Words : Astrocytoma; Cerebellum

Pleomorphic xanthoastrocytoma (PXA) is a rare tumor that generally occurs in the second to fourth decade of life.[1,2] Only five cases have been reported in the cerebellum so far, and four of them were composite PXA-gangliogliomas.[3] The differential diagnosis of PXA primarily includes ganglioglioma, glioblastoma, desmoplastic infantile ganglioglioma, monstrocellular sarcoma, and malignant fibrous histiocytoma.

CASE REPORT

A 49-year-old female was admitted to the emergency department with a four-month history of headache and dizziness. On the neurological examination at admission, an ataxic gait and an abnormal left finger-to-the nose test were observed. A computerized tomogram revealed a well enhancing solid mass that included a cystic component in the cerebellar vermis with associated obstructive hydrocephalus. Magnetic resonance imaging showed a $4.0 \times 3.5 \times 3.0$ cm mass lesion that had both solid and cystic components with surrounding edema in the midline of the cerebellar hemisphere near the fourth ventricle (Fig. 1).

The patient underwent total gross removal of the brain tumor via suboccipital craniotomy. During the surgery, a brownish red, slightly vascular, soft tumor was found in the cerebellar vermis and it was compressing the fourth ventricle. The tumor had a solid portion and a cystic portion that contained light yellow fluid; it was not associated with necrosis or hematoma. This tumor was composed of fibrillary, giant, often multinucleated neoplastic astrocytes and large xanthomatous cells (Fig. 2). The tumor cells had abundant eosinophilic granular cytoplasm and they showed intracellular accumulation of lipids. Eosinophilic granular bodies were also found between the neoplastic cells (Fig. 3). There was a focal collection of reactive lymphocytes. A pericellular and lobular reticulin pattern was present (Fig. 4). Immunohistochemically, many of the tumor cells showed positive reactivity for glial fibrillary acidic protein (GFAP; ZCG29; Zymed,

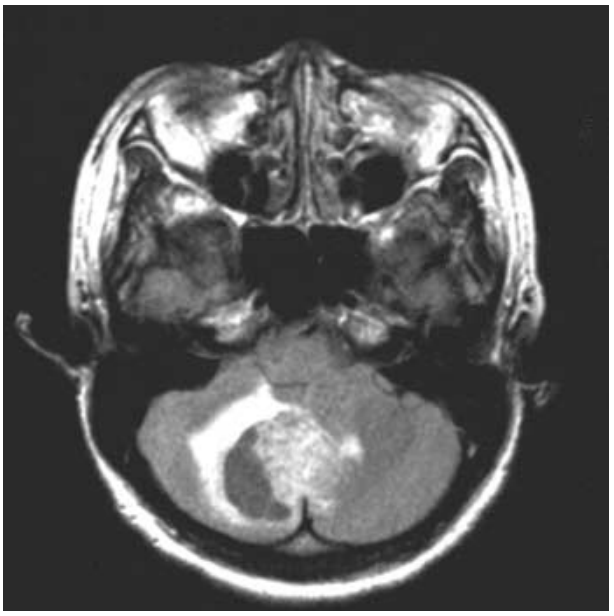

Fig. 1. Brain MRI shows a mass lesion having a solid and cystic component with a surrounding edema in the midline of the cerebellar hemisphere near the fourth ventricle.

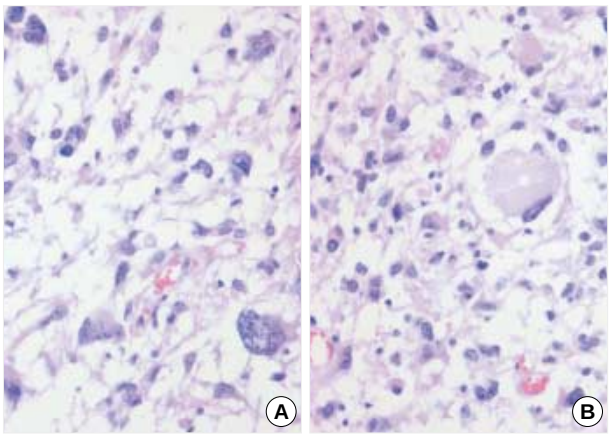

Fig. 3. The tumor consists of mononuclear and multinucleated neoplastic astrocytes showing nuclear and cytoplasmic pleomorphism (A). The tumor cells have abundant eosinophilic granular cytoplasm and some show intracellular lipid (B).

CA, USA) (Fig. 5) and S-100 protein (polyclonal; DakoCytomation, Copenhagen, Denmark). The Ki-67 (B56; BD PharMingen, CA, USA) labeling index was less than 1%. This tumor showed marked cellular pleomorphism, but there were no definite findings of anaplasia, endothelial cell proliferation, mitoses or necrosis. A diagnosis of PXA was made based on the tumor's histopathology features. Neither radiation nor chemotherapy was administered. The postoperative course was uneventful during 8-months of follow up.

Fig. 2. Low magnification shows leptomeningeal involvement of tumor with focal invasion into cerebellar cortex. Perivascular infiltration of lymphocytes is also noted.

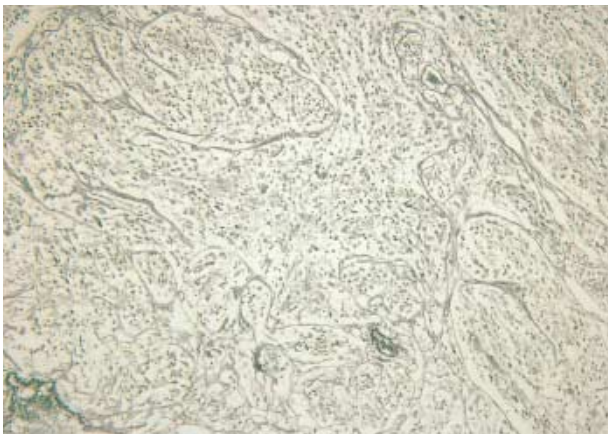

Fig. 4. Special stain for reticulin fiber shows reticulin networks surrounding individual cells or groups of tumor cells.

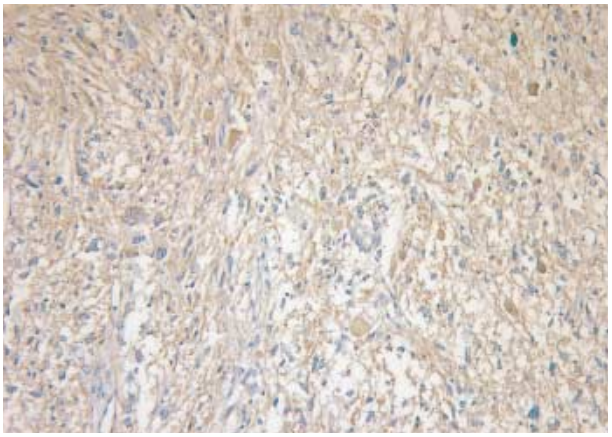

Fig. 5. Immunohistochemical stain for glial fibrillary acidic protein shows diffuse positive reaction in tumor cells.

DISCUSSION

PXA is a low-grade astrocytoma that corresponds to WHO grade II.[4] Males and females are equally affected. The majority of PXA cases occur in a supratentorial location within the temporal or parietal lobe, and they are often associated with cyst.[5-8] The occurrence of PXA outside the cerebral hemisphere is very rare. Tumor in a supratentorial location is revealed in the majority of cases by epileptic seizures, and such a tumor is less frequently revealed by neurological deficits or intracranial hypertension. This type of tumor is sometimes heralded by childhood seizures with the later emergence of mass effects.[9] Yet our case developed in the cerebellum with the main symptoms of headache and dizziness, and these symptoms are usually presented with cerebellar tumor.

Imaging studies frequently demonstrate a cystic component and an enhancing nodule that is associated with a variable degree of surrounding edema and a mass effect. The solid portion of the tumor appears inhomogeneously hypo dense or hyper dense on the computerized tomogram, while it usually is hypo-intense or iso-intense on the T1-weighted magnetic resonance images, and it's hyperintense to the parenchyma on the T2-weighted images. Angiography usually shows a hypovascular mass, although a blood supply from the external carotid artery may be observed.

On gross examination, PXA appears as a firm mass or as a mural nodule projecting into a cyst filled with clear or amber proteinaceous fluid. The cystic component does not represent necrotic tissue. The wall of the cyst consists of reactive glial cells. The "typical" PXA consists of spindle-shaped cells with elongated nuclei, and there are enlarged, bizarre cells with intracytoplasmic lipid vacuoles and multilobulated or multiple nuclei.[10] Mitoses, if they are present, are infrequent, and necrosis is absent. Other features include lymphocytic perivascular cuffing, granular eosinophilic droplets and a reticulin-rich stroma. The rich reticulin network plays a role in creating the impression of a mesenchymal tumor, particularly in the areas where individual tumor cells are surrounded by reticulin fibers. An evident reticulin network surrounds the individual cells or small nests of cells; this feature is attributable, in part, to the production of the basal lamina by the tumor cells. In spite of the presence of reticulin, collagen depositions, (hemi) desmosomes, and intracytoplasmic lipid droplets, the strong GFAP positivity of the tumor cells was seen as a definite sign of the true glial nature of this tumor.[11] The ultrastructural features of PXA include intracytoplasmic lipid and intermediate filaments, incomplete cell junctions and a surrounding basal lamina. On the other hand, in rare instances, a high mitotic activity, marked hypercellularity and necrosis may be found in the initial tumor as well as in the specimens from the recurrent tumors. The PXA showing these histological anaplastic features can be simply designated as "atypical" and it must be distinguished from glioblastoma.[7] The PXA with anaplastic features shows high mitotic activity ($\geq$5 mitosis per 10 HPF) with or without accompanying necrosis.[12] The presence of pericellular reticulin staining, as well as the absence of vascular hyperplasia and nuclear pseudopalisading, are highly suggestive for "atypical" PXA and so this would exclude the diagnosis of glioblastoma.[7]

PXA generally follows an indolent course with gross total resection being the treatment of choice. The prognosis is generally good with a good functional outcome; however, anaplastic transformation has been documented.[13] At present, the role of adjuvant radiotherapy and/or chemotherapy remains uncertain. One might extrapolate from the current management recommendations to administer external beam radiation therapy for those patients with postoperative residual tumor and for the tumors that are thought to have "anaplastic" features. Histologic malignancy in PXA does not correlate with the prognosis as reliably as that for patients with ordinary, diffuse astrocytoma. The clinical course of patients with histologically malignant PXA was often more favorable and less precipitous than that of the patients with fibrillary astrocytomas that showed the same features.[12] Analysis of the published data reveals that the 5-year survival rate for the patients harboring "typical" PXA is approximately 80%. None of the patients with "atypical" PXA have been reported to survive for more than 3 years. A "typical" PXA is associated with a relatively favorable course, while the "atypical" PXA has a much worse prognosis that falls into an intermediate grade between "typical" PXA and glioblastoma.[7] For slowly growing tumor such as PXA, which has an inherently good prognosis, more cases and longer periods of follow-up will be essential to confirm or refute our findings. In fact, a "registry" approach to such uncommon tumors may be the only way for such a knowledge base to expand.[12]

We report here on a case of PXA in the cerebellum. This rare tumor should be included in the differential diagnosis of cerebellar neoplasms and it is worthy of attention in regards to its histological and immunohistochemical findings.

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